Correspondence

Dietary Fat and Coronary Disease

SIR,—Your leading article (*Journal*, July 13, p. 89) admirably summarizes present knowledge about the effect of different fat-containing diets and cholesterolaemia and coronary thrombosis. Discussing blood coagulation, you comment that "the picture is far from clear." May I attempt to clarify some small parts of the picture?

Your leader says, "It has still to be proved that the hypercholesterolaemia causes faster blood coagulation." Changes in some blood coagulation tests have been reported only in the immediate post-prandial period. Throughout the digestion of a single meal the cholesterol level in the blood remains unchanged. Under these conditions cholesterol presumably plays no part in any clotting changes observed. No investigations of blood coagulability have been undertaken following prolonged fat feeding of sufficient duration to produce changes in the blood cholesterol. Fullerton *et al.*[1] claimed that there was a shortening of the clotting time of whole blood in a silicone-coated test-tube after a single fatty meal. Merskey *et al.*[2] also gave single fatty meals and did not give "low and high fat diets." This claim has been confirmed[3–5] and denied.[2 6–8] Most workers would agree that this apparently simple test is, in practice, extremely sensitive to minute uncontrollable variations in technique and that closely reproducible results are never obtained. The discrepancies mentioned above may, therefore, be attributable to differences in technique. Such a test, with its great inherent variability, is largely unsuitable to reveal any but major changes in the coagulability of the blood. Since the facts are still in doubt, it is profitless at this juncture to discuss their implications.

Merskey *et al.*[2] did not record that "the stypven time of the *blood* of patients on the high fat *diet* was lower than that of blood from patients on a low fat diet" (my italics). They used the Russell viper venom accelerated clotting time of platelet-poor plasma—the "stypven" time—and observed the effect of single meals. They found a significant acceleration in the stypven time four hours after a high-fat meal, but no change after a low-fat meal, or when no fat was given. This test, unlike the clotting time of blood, is highly reproducible, and, in fact, there is general agreement with this observation.[1 2 9–11]

Since thrombocytopenic people are rarely bitten by *Vipera russelli* after eating a large fatty meal, the significance of this empirical test in normal physiology is not immediately apparent. This acceleration of the stypven time may be due to an increase in free fatty acids,[12] but is more likely to be due to an increase in the available active phospholipids in the blood.[10 13 14] Even if the latter view is correct, it is not known if such an increase is of physiological importance, although, clearly, it might be.[15] It has, however, been shown[16] that after physiological quantities of different fats in many tests there was no demonstrable difference between 20 male patients with proved coronary thrombosis and 20 volunteers of the same age and sex. This suggests either that the immediate post-prandial effects of a fatty meal are not relevant to the causation of coronary thrombosis or that the *wrong* tests have been performed: blood coagulation studied in the test-tube may have little relevance to the *in vivo* formation of a thrombus. The former view is strengthened by the observation[17] that the incidence of coronary disease throughout the day and night is fairly constant, and had post-prandial lipaemia been a factor the incidence would surely have dropped between 12 p.m. and 6 a.m.—I am, etc.,

Portsmouth. J. R. O'BRIEN.

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Infection in Xenopus laevis with Human Group A Streptococcus

SIR,—We wish to report an example of a human type streptococcus causing an outbreak of disease in a colony of amphibia kept in the Department of Pharmacology, Welsh National School of Medicine, Cardiff. Two years ago, during the very hot summer weather, an epidemic struck the colony of *Xenopus laevis* in this school. The death rate was high and the pattern of attack was always the same. The toads affected were females being used in routine pregnancy tests. After an injection the toads seemed normal, and then about three days later they were seen to be floating on the surface. Twenty-four hours afterwards the toads were dead. Every animal had a bloated appearance and there were small petechiae on the breast. Fluid withdrawn from the toad had a milky appearance, and on culture a growth of streptococci was obtained. At the time, this observation was not followed further.

This outbreak decimated the stock and certain precautions were taken. The staff were swabbed and were found to be negative. The temperature of the circulating water was dropped to about 17° C. and the artificial heating in the amphibia room was turned off. Every tank was scrubbed with a strong lysol solution. However, the animals continued to die until the general temperature dropped from the higher summer values to more or less normal autumnal figures.

During the next two years there have been sporadic cases and each time the symptomatic picture has been the same. Direct microscopical examination of the fluid in every instance demonstrated the presence of very numerous Gram-positive cocci, in long and short chains, having the morphological appearance of streptococci. Cultures of the lymph sac fluid from nine infected toads were made, and in each case a group A streptococcus was isolated. Typing of the organism showed it in all cases to be 3/13/B3264. The disease was not limited to those toads which had been recently injected with human urine for pregnancy diagnosis, but also occurred in toads which had not been used for some months. The affected animals showed an extreme degree of septicaemia, and a direct-film examination of blood showed large numbers of streptococci. Some animals were treated with 100,000 units of soluble penicillin daily into the dorsal lymph sac with excellent results.

We should like to thank Mr. H. Price and Mr. M. Jones, of the Public Health Laboratory, Cardiff, for valuable technical assistance.—We are, etc.,

R. W. S. HARVEY.
Cardiff. G. M. MITCHELL.

Dangers of Cigarette-smoking

SIR,—In the *Journal* of July 20 (p. 158) Dr. Robert N. C. McCurdy writes, "Fisher's criticism (*Journal*, July 6, p. 43) . . . would not be so unfair if he had specified what alternative explanations of the facts still await exclusion." I had hoped to be brief. A few days later the B.B.C. gave me the opportunity of putting forward examples of the two classes of alternative theories which any statistical association, observed without the precautions of a definite experiment, always allows—namely, (1) that the supposed effect is really the cause, or in this case that incipient cancer, or

a pre-cancerous condition with chronic inflammation, is a factor in inducing the smoking of cigarettes, or (2) that cigarette-smoking and lung cancer, though not mutually causative, are both influenced by a common cause, in this case the individual genotype.

The latter unexcluded possibility was known to Dr. McCurdy, but he brushes it aside with abundant irony. Is he really persuaded that this is the way to arrive at scientific truth? Dr. McCurdy points out correctly that difference in the genotypic composition of the smoking classes—non-smokers, cigarette smokers, pipe smokers, etc., would not explain the secular change in lung-cancer incidence. I had never thought it would be charged with this task. Is it axiomatic that the differences between smoking classes should have the same cause as the secular change in incidence? Is there the faintest evidence to support this view? Indeed, Dr. McCurdy's belief that cigarette-smoking causes lung cancer would be more secure if he did not encumber it with the *non sequitur* that increase of smoking is the cause of increasing cancer of the lung. For at this point there appears one of those massive and recalcitrant facts which have been emerging through the smoke-screen of propaganda. When the sexes are compared it is found that lung cancer has been increasing more rapidly in men relatively to women. The absolute rate of increase is, of course, obscured by improved methods of diagnosis, and by the increased attention paid to this disease, but the relative proportionate changes in men and women should be free from these disturbances, and the change has gone decidedly against the men. But it is notorious, and conspicuous in the memory of most of us, that over the last 50 years the increase of smoking among women has been great, and that among men (even if positive) certainly small. The theory that increased smoking is "the cause" of the change in apparent incidence of lung cancer is not even tenable in face of this contrast.

For the secular change, therefore, neither the smoking-causation theory nor the theory of differentiated genotype will afford an explanation. For the contrast between cigarette smokers and non-smokers both are available; for the contrast between cigarette smokers and pipe smokers the first theory requires some special pleading, but this has never been lacking. The two circumstances, (1) that heavy smokers show a greater effect than light smokers, and (2) that persons who have voluntarily abandoned smoking react like non-smokers or light smokers, are not independent experimental confirmations of the smoking theory. They are only reiterations of the main association to be explained. Any theory which explains this association may be expected to explain these facts also.

Differentiation of genotype is not in itself an unreasonable possibility. Inbred strains of mice if genotypically different almost invariably show differences in the frequency, age-incidence, and type of the various kinds of cancer. In man cancer of the stomach has been shown to be favoured by the gene for the blood group A. My claim, however, is not that the various alternative possibilities which have not been excluded all command instant assent, or are going to be demonstrated. It is rather that excessive confidence that the solution has already been found is the main obstacle in the way of such more penetrating research as might eliminate some of them. I am sure it is useless to treat the question as though it were a matter of loyalty to a political ideology or of forensic disputation. Statistics has gained a place of modest usefulness in medical research. It can deserve and retain this only by complete impartiality, which is not unattainable by rational minds. We should not be content to be "not so unfair," for without fairness the statistician is in danger of scientific errors through his moral fault. I do not relish the prospect of this science being now discredited by a catastrophic and conspicuous howler. For it will be as clear in retrospect, as it is now in logic, that the data so far do not warrant the conclusions based on them.—I am, etc.,

Cambridge. RONALD A. FISHER.

Smoking and Lung Cancer

SIR,—Medical research bodies in America, England, Australia, and elsewhere have arrived at the conclusion that the increase in cancer of the lung is linked with the use of tobacco, and that there are proportionately more cases of lung cancer among those who smoke more than 20 cigarettes daily than among those who smoke less than this or do not smoke at all. There are numerous varieties of tobacco, and it is possible that they may not all have the same effect on human beings.

In the past Anatolian tobacco was smoked in large quantities in Europe, and there were not so many cases of cancer of the lung as there are now. Why does tobacco now affect the lungs more than it used to? Is it because of the change from Anatolian tobacco to the almost universal use of Virginian? Before the first world war, Europeans, and particularly Anatolians, smoked Anatolian tobacco; even the Americans used a blend containing a good proportion of this variety. After that war Virginian tobacco rapidly displaced Anatolian. After the second world war Virginian tobacco dominated the market, and where Anatolian was not entirely displaced the proportion of Virginian in the blend increased. Cancer of the lung has rapidly followed this dominance by Virginian tobacco.

Here is an important point for inquiry by research workers. I consider it advisable that they should study carefully and impartially the carcinogenic properties of both Virginian and Anatolian tobacco. The components of both these varieties are different, and therefore their effect may be different.—I am, etc.,

Famagusta, Cyprus. ANTONIS GEORGEADES.

The Forgotten Thomas Splint

SIR,—Mr. G. P. Arden's letter (*Journal*, July 13, p. 101) will surely be welcomed by surgeons throughout the country, and should be appreciated by all concerned with the transport of casualties. In this county, where accident cases must travel long distances to hospital, an effort is being made to re-establish the use of the Thomas splint. By agreement with the local medical committee, Thomas adjustable splints (each with three rings) and weatherproof stretchers with suspension bars have been placed at strategic points throughout the county for use by doctors, police, and trained Red Cross personnel.—I am, etc.,

Golspie, Sutherland. B. SOUTAR SIMPSON.

SIR,—It was surprising to learn from Mr. G. P. Arden's letter in your columns (*Journal*, July 13, p. 101) that it is still necessary to reiterate the merits of the Thomas splint. One would have thought, as he has said, that a method of treatment which in 1916 reduced the immediate mortality due to open fractures of the femur from 80% to 20% within a few weeks of its introduction into the front line needed no further advocacy. The long Liston splint in such cases is inadequate and even dangerous. A broken femur is difficult to control by any splint, because the bone is contained within a deep mass of muscle. Liston's splint, lacking the all-important traction element of Thomas's, can hold such a fracture only if it is so firmly bandaged to the limb as to further endanger a circulation often already in jeopardy. Any swelling which occurs after the splint has been applied will obviously still further increase the risk of serious ischaemia. And, apart altogether from these considerations, the splint itself (which extends to the axilla) is uncomfortable in the extreme, and renders it difficult to transport a patient save on an absolutely rigid stretcher.

One feels that one justifiable objection to the Thomas splint in the past has been the difficulty encountered in fitting a splint of the correct size to any given patient, whatever the dimensions of his thigh. R.A.M.C. units carry three different sizes, and one of this range can be found to fit most adult males. Civilian casualty organizations must be prepared to treat women and children as well, and a